## REMARKS

Claims 1 to 18, 21 to 25, 27, 41, 44, 47, 49, 50 and 52 are under examination in this application. Claims 28 to 40 were previously withdrawn as directed to a non-elected invention. Claim 26 was previously cancelled without prejudice. Claim 19 has been cancelled herein without prejudice.

Claims 1, 2, 4, 8, 10, 11, 14, 15, 21, 23, 25, 41, 44, 47, 49, 50 and 52 have been amended for clarity to more particularly define the invention. Support for these amendments is found throughout the specification and in the original claim language as set forth below. Support for the amendments to claims 1, 2, 21 and 23 can be found at page 15, last full paragraph, and elsewhere in the application, as filed. No new matter is added by these amendments and their entry is respectfully requested. In light of the amendments presented herein and the following remarks, Applicant respectfully requests reconsideration of the pending application and allowance of the pending claims to issue.

### Interview Summary

Applicant thanks the Examiner for the courtesy of the telephone interview on March 29, 2005 with participants Yahia Gawad, Nelson Yang, Long Le, David Heller and Charles Boulakia.

During the telephone interview, Yahia Gawad, the inventor, discussed resetting the photomultiplier between the time of (a) effecting calcium release from the calcium-caging compound and (b) measuring luminescence by the calcium-sensitive luminescent material with the photomultiplier. The inventor further discussed the distinctions regarding the calcium concentrations as discussed in the cited reference in contrast to the calcium

concentration employed in the present invention. In particular, the inventor noted that the invention described in Liotta et al. would not perform the desired function given the concentrations of calcium Liotta et al. indicates in the solution, and the ability of calcium-caging compounds to release that amount of calcium in a short enough period of time that the two light signals would not coincide.

Although an agreement was not reached regarding passing the pending claims to allowance, the Examiner indicated that the inventor's comments and proposed amendments would be considered in a response to the pending Office Action in the above-referenced matter. Amendments and remarks in view of the telephone interview are incorporate herein.

**Rejection under 35 U.S.C. §112**

The Examiner has rejected claim 1 under 35 U.S.C. §112, first paragraph, as failing to comply with the written description requirement. Specifically, the Examiner states that the claim contains subject matter which was not described in the specification in such a way as to reasonably convey to one skilled in the art that the inventor had possession of the claimed invention at the time the application was filed. Specifically, the Examiner has stated that, while the Applicant discloses the selection of a calcium sensitive chemiluminescent material to obtain a short period of time between the flash emitted by the ultraviolet light source and the emission of light by the calcium-sensitive luminescent material (as seen in page 15), the Applicant does not disclose the selection of calcium caging compound for this purpose. *See* Office Action, pages 2-3.

In an effort to expedite prosecution of the present application, Applicant has amended claim 1 as presented above. Specifically, Applicant has removed the selection of calcium caging compound for this purpose. Applicant has also amended claims 21 and 23 in a similar fashion. Finally, Applicant has added the "wherein" language found in claims 1, 21 and 23 to claim 2, since claim 2, as amended, is no longer dependent on claim 1.

**Rejection under 35 U.S.C. §103**

The Examiner has rejected claims 1-7, 10-12, 14-17, 19, 21-25, and 27 as being obvious over Pankratz et al. [US 5,876,935] in view of Liotta et al. [US 5,942,407]. Specifically, the Examiner states that, with respect to claims 1, 2, 21, 23, and 25, Pankratz et al. teach a method comprising the steps of combining with a sample a binding reagent labeled with a luminescent molecule that is capable of binding to an analyte, contacting the sample with another binding reagent that can be biotinylated, immobilized on a solid support such as superparamagnetic microspheres by means of avidin or streptavidin, so that a complex with the analyte bound to the labeled binding reagent is formed, activating the luminescent label in the solid support-free sample or in the complex bound to the solid support, and determining the presence of analyte in the sample by detecting the light emitted from the activated luminescent label. *See* Office Action, page 3. The Examiner states that Pankratz et al. further teach that the label can be aequorin, and is activated by adding sufficient calcium ions. *See* Office Action, page 3. The Examiner concedes that Pankratz et al. fails to teach that the calcium ions are added by using ultraviolet light to effect the release of calcium from a caged calcium compound. *See* Office Action, page 4.

The Examiner further states that Liotta et al. teaches the use of a caged calcium compound immobilized in a support and using ultraviolet light to activate the compound in order to extend the duration of light emission resulting from analyte detection. *See* Office Action, page 4.

The Examiner therefore contends that it would have been obvious to include a caged calcium compound immobilized in a support and ultraviolet light to activate the compound in the method of Pankratz et al., in order to extend the duration of light emission resulting from analyte detection. *See* Office Action, page 4.

The Examiner has also stated that while neither Liotta et al. or Pankratz et al.teach that the calcium-sensitive luminescent material is selected to obtain a period of time between the flash emitted by the ultraviolet light source and the emission of light by the calcium-sensitive luminescent material, the calcium-sensitive luminescent material used by both Liotta et al. and Pankratz et al. is aequorin, and therefore, such a period of time would be present in the method of Pankratz et al. in view of Liotta et al. *See* Office Action, page 4.

The Examiner does acknowledge that the prior art does not teach that there is a period with no light emission between the pulse of ultraviolet light effecting calcium release and the emission of luminescence by the luminescent material. *See* Office Action, page 4.

Liotta et al. do not use a caged calcium compound to activate a calcium-activated luminescent material. Instead, Liotta et al use a calcium salt. In Liotta et al., calcium is released into the solution when the calcium salt is hydrated. Liotta et al. do not show examples utilizing a caged calcium

compound, and do not anticipate the problems related therein – specifically, that the calcium caged within the caged calcium compound is triggered with light. Liotta et al. is flawed and thus teaches away from the present invention. Liotta et al. describes that 10 to 100 mM of calcium is necessary to trigger the calcium activated luminescent material. Therefore, Applicant respectfully submits that one of ordinary skill in the art would not select the method of Liotta et al. for use with calcium caging compounds, since, to have that much calcium released from the calcium caging compounds, there would inevitably be some 'bleeding' of calcium from those compounds and it is unlikely to have that much calcium released and not have a level of free calcium below 20nM before the activation of the caging compounds. As the Applicant teaches, free calcium levels above 20 nM would prematurely activate the calcium activated luminescent material. Liotta et al. do not teach how to use caging compounds to release calcium in amounts sufficient to emit light from calcium activated luminescent material. In addition, applying Liotta et al. to Pankratz et al.would not be practical in whole blood; as provided in the present disclosure, the blood cells and the free calcium are removed from the solution in the method described therein.

Finally, none of the cited references describe how to use a photomultiplier tube to collect light from calcium activated luminescent materials, when a UV light source of enough power to release calcium from calcium caging compounds is used to stimulate light generation from calcium activated luminescent materials.

Embodiments of the current invention disclose how to differentiate between the light emitted to activate the caged calcium compound, and the light emitted by the calcium-sensitive luminescent material. Neither

Pankratz et al. nor Liotta et al. disclose resetting the photomultiplier (used for measuring the light emitted by the calcium-sensitive luminescent material) between the time of the light activation of the caged calcium compound and the resulting activation of the calcium-sensitive luminescent material. Indeed, neither the problem solved nor the advantage obtained in resetting the photomultiplier is taught or suggested by the cited references. This step is taught at page 15, lines 19-30 of the present application and recited in the present claims, as amended. Applicant submits that the claims, as amended are thus novel and non-obvious over the cited references for at least the reasons set forth.

Applicant has amended claims 1, 2, 21 and 23 to add a recitation directed to resetting the photomultiplier between the ultraviolet light source emission and the emission of light by the calcium-sensitive luminescent material. Support for this recitation can be found at page 15, lines 19-30. Applicant respectfully submits that, due to their respective dependence on claims 1, 2, 21 or 23, the Examiner's rejection of claims 3-7, 10-12, 14-17, 22, 24-25 and 27 have also been addressed. Claim 19 has been cancelled by the Applicant without prejudice.

The Examiner has rejected claim 26, stating that Liotta et al. teach that the timing of the caged calcium can extend the length of the light pulse, and provides a technique for performing multiple assays at once. Applicant respectfully submits that this rejection has been obviated, since claim 26 was cancelled without prejudice in the Applicant's last communication with the Patent Office.

The Examiner has rejected claims 41-48, stating that it has been held that where the general conditions of a claim are disclosed in the prior art,

discovering the optimum or workable ranges involves only routine skill in the art, and therefore it would have been obvious through normal optimization techniques known in the art to load the calcium-caging compound with up to 75% calcium, and for the free calcium concentration of the solution to be less than 20 nanomolars. *See* Office Action, page 6. Applicant respectfully submits that since these claims are dependent on claims 1, 2, 21, or 23, this rejection has been addressed in amendments to those claims, as described above.

The Examiner has rejected claims 8, 9, 13, 18, 20 and 49-54 as unpatentable over Pankratz et al. in view of Liotta et al. and further in view of Ellis-Davies et al. [US 5,446,186]. Specifically, the Examiner has stated that, with respect to claims 13 and 49-54, Pankratz et al. and Liotta et al. teach a method of a binding assay as discussed above involving the use of aequorin and obelin and of caged calcium compounds. *See* Office Action, page 6. Though the Examiner concedes that neither Pankratz et al. nor Liotta et al. teach specific caged calcium compounds, he states that Ellies-Davies et al. does teach DM-nitrophen and NP-EGTA as well known in the art as calcium chelating compounds. *See* Office Action, page 6. The Examiner contends that it would therefore have been obvious to use DM-nitrophen or NP-EGTA as the caged calcium compounds in the method of Pankratz et al. and Liotta et al., as described previously. *See* Office Action, page 7.

The Applicant respectfully submits that the amendments to claims 1, 2, 21 and 23 (from which claims 13 and 49-54 depend) obviatethese rejections.

The Examiner has rejected claims 8, 9, 18 and 20, stating that Liotta et al. teaches the use of ultraviolet light, which can be in the form of a light pulse, to activate the caged calcium compound. Ellis-Davies et al. further

specify the use of a laser at 347 nm to liberate the calcium. *See* Office Action, page 7. Finally, Liotta et al. describes use of a photomultiplier to sense the luminescence of aequorin. *See* Office Action, page 7.

The Applicant respectfully submits that the amendments to claims 1, 2, 21 and 23 (from which claims 8, 9, 18 and 20 depend) obviate these rejections.

**Amendments to Claims Not Specifically Addressing Examiner's Rejections**

The Applicant has further amended certain claims to better define the ambit of protection sought.

The recitations directed to the elongated matrix and transverse stripe have been deleted from claims 1, 2, 21, 23 and corresponding dependent claims.

Recitations from claim 1, from which claim 2 depended, have been added to claim 2, which has been made into an independent claim. Correspondingly, claims dependent on claim 1 are now dependent on claims 1 or 2.

Claim 5 has been amended to better define the invention.

Claim 8 has been amended to remove recitations now incorporated into claims 1 and 2.

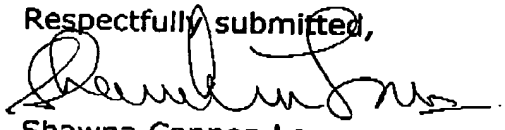
Claims 14 and 15 have been amended to clarify the invention.

Favourable reconsideration and allowance of this application are respectfully requested.

Should the Examiner believe, however, that additional amendments to the claims may be required to secure allowance of this application; he is invited to telephone the undersigned to facilitate allowance of this application.

It is not believed that any fee(s), including fees for additional claims, are required, beyond those that may otherwise be provided for in documents accompanying this paper. In the event, however, that additional fees are necessary to allow consideration of this paper, such an extension is also hereby petitioned for under 37 C.F.R. §1.136(a). Applicants authorize that any additional fees believed to be due in connection with this paper may be charged to Deposit Account No. 50-0220.

Respectfully submitted,



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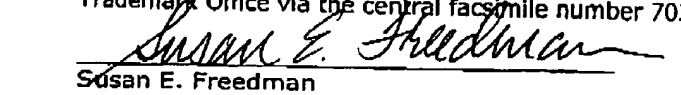

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